

Remarks/Arguments

Claims 1 and 3-15 are pending in the application; claims 3, 4, 6 and 8-13 have been withdrawn. Claim 15 is canceled herein. Accordingly, claims 1, 5, 7, and 14 are presented for examination on the merits.

I. Rejection of Claim 15 Under 35 USC § 112, First Paragraph (Written Description)

The rejection of claim 15 is respectfully rendered moot by the cancellation of that claim.

II. Rejection of Claims 1, 5, 7, 14 and 15 Under 35 USC § 112, First Paragraph

Claims 1, 5, 7, 14 and 15 are rejected under 35 USC § 112, first paragraph. The Examiner asserts that the specification does not enable the full scope of the claims. Specifically, the Examiner asserts that the specification does not enable a method of preventing hypertension.

This rejection is respectfully traversed as follows.

The data presented in Figures 3A and 3B demonstrate that the xanthine oxidase inhibitor, allopurinol, prevents hypertension in a rat model of the disease. Control rats placed on a mild salt restriction diet have a fall in blood pressure after several weeks. This is prevented when the diet also contains oxonic acid, which is shown in Figure 2 to elevate blood pressure in rats. However, rats placed on diets containing oxonic acid, low salt and allopurinol, do not show an increase in blood pressure, *i.e.*, hypertension was prevented. Thus, the present specification enables claims to methods of both preventing and treating hypertension using a xanthine oxidase inhibitor of the invention.

Accordingly, the rejection of claims 1, 5, 7, 14 and 15 under 35 USC § 112, first

paragraph is respectfully traversed.

III. Rejection of Claims 1 and 5 Under 35 USC § 112, First Paragraph

Claims 1, 5, 7, 14 and 15 are rejected under 35 USC § 112, first paragraph. The Examiner asserts that the specification does not enable the full scope of the claims and maintains that Applicant has not provided sufficient evidence that the class of compounds known as xanthine oxidase inhibitors will act to treat hypertension.

Applicant disagrees with the Examiner's conclusion.

The specification teaches that there is a link between high serum uric acid levels and high blood pressure. The specification also provides evidence of the deleterious effects of high serum uric acid levels on blood pressure and demonstrates that these deleterious effects are prevented or successfully treated by administration of a known xanthine oxidase inhibitor, allopurinol. Applicant has also cited the Merck Index which discloses that allopurinol is a member of a well known class of compounds that lower uric acid levels. [See Merck Index, pp. 52 and 53, of record].

Applicant has previously provided a published review article, Hayden and Tyagi, Nutrition and Metabolism 2004, 1:10, which discloses that there is a link between high uric acid content and hypertension and suggests four potential mechanisms involved in the association between hyperuricemia and hypertension [page13, section entitled "Hypertension"]. Among the potential mechanisms is increased xanthine oxidase production, which ultimately results in increased levels of oxidative-redox stress [page 14]. The review article also cites three references (all published in 2002 or later) that demonstrated administration of an xanthine oxidase inhibitor, either allopurinol or

oxypurinol, reversed the production of superoxide (reactive oxygen species), returning the system to production of nitric oxide, which reduces oxidative–redox stress. [page 14] Thus, this review article provides further evidence that other xanthine oxidase inhibitors, *e.g.*, oxypurinol, have the same effect as allopurinol, and further demonstrates that allopurinol is a member of a class of compounds that have the claimed effect on hypertension.

It is also evident from the disclosure of the previously filed review article that a link between high uric acid levels and hypertension is known, and there are several organic defects that can lead to increased uric acid content and hypertension [Hayden and Tyagi, page 14]. Applicant has discovered that use of compounds that lower uric acid levels, xanthine oxidase inhibitors or other uric acid lowering compounds, is sufficient to lower blood pressure. Thus, the specification provides an enabling disclosure for use of the claimed class of compounds which are known in the art to lower uric acid levels.

A specification which contains a teaching of how to make and use claimed subject matter *must* be taken as enabling unless there is a reason to doubt the objective truth of the statements relied upon in the specification. *In re Brana*, 51 F.3d 1560, 1566 (Fed. Cir. 1995) (emphasis in original; citing *In re Marzocchi*, 439 F.2d 220, 223 (CCPA 1971)). Further more, the enablement standard is an objective standard and it is irrelevant whether the teaching in the specification is accomplished by broad terminology or illustrative examples. *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). In fact there is requirement that a working example be provided. *In re Strahilevitz*, 668 F.2d 1229, 1232 (CCPA 1982)..

The Examiner has not met his burden of showing that the claims exceed the scope of enablement. In particular, the Examiner has not offered any evidence or reason to doubt that xanthine oxidase inhibitors, as a general class of compounds, do not have the same mechanism of action as allopurinol.

Accordingly, the rejection of claims 1, 5, 7 and 14 under 35 U.S.C. § 112, first paragraph, is respectfully traversed.

IV. Rejection of Claim 15 Under 35 USC § 112, First Paragraph (Enablement)

This rejection is rendered moot by cancellation of claim 15.

V. Rejection of Claims 1 and 5 Under 35 USC § 102(b) Over Baldwin

Claims 1 and 5 are rejected under 35 USC § 102(b) as allegedly being anticipated by Baldwin (US 4,058,614). The Examiner states that Baldwin discloses the use of imidazole compounds, which are xanthine oxidase inhibitors, for the treatment of hypertension.

This rejection is respectfully traversed as follows.

Baldwin is directed to the use of imidazole derivatives which are useful as anti-hypertensive agents **or** xanthine oxidase inhibitors. *See* Abstract, column 1, lines 21-25, and claims 14 and 7. No where in this patent is it disclosed that any of the compounds are both xanthine oxidase inhibitors **and** hypertensive agents. Furthermore, this reference does not suggest that any of the disclosed imidazole derivatives both inhibits xanthine oxidase and has anti-hypertensive activity. Thus, contrary to the Examiner's assertion, this patent does not disclose the presently claimed invention, *i.e.*, the use of

xanthine oxidase inhibitors to treat or prevent hypertension.

Accordingly, the rejection of claims 1 and 5 under 35 USC § 102(b) over Baldwin is respectfully traversed.

V. Rejection of Claims 1, 5, 7, 14 and 15 Under 35 USC § 102(b) Over Miyamoto et al.

Claims 1, 5, 7, 14 and 15 are rejected under 35 USC § 102(b) as allegedly being anticipated by Miyamoto et al. The Examiner states that Miyamoto et al. discloses the inhibition of xanthine oxidase by pyrazolpyrimidine derivatives. The Examiner also states that Miyamoto discloses administration of allopurinol to rats with a resulting decrease in blood pressure. The Examiner concludes, therefore, that the cited reference anticipates the present claims.

This rejection is respectfully traversed as follows.

Miyamoto discloses that administration of allopurinol to rats results in a transient decrease in blood pressure. However, this disclosure does not anticipate the claimed invention. The fact that Miyamoto demonstrated that allopurinol provides only a transient decrease in blood pressure **is a teaching away from the claimed invention**. A transient decrease in hypertension indicates that the drug, allopurinol, **does not work** to prevent or treat hypertension. Thus, the cited reference does not disclose the use of a xanthine oxidase inhibitor, *i.e.*, allopurinol, to treat or prevent hypertension, but instead teaches that allopurinol cannot be used to treat or prevent hypertension.

Accordingly, the rejection of claims 1, 5, 7, 14 and 15 under 35 USC § 102(b)

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over Miyamoto et al. is respectfully traversed.

It is respectfully submitted that the present application, with claims 1, 5, 7, 14 and 15 is in condition for allowance, an early notification thereof being earnestly solicited.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

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